#### REMARKS

Claims 1-69 were originally presented in the present application. Claims 33-55 have been cancelled pursuant to a restriction requirement and without prejudice to Applicants' rights to pursue these claims in other patent applications. Claims 1-32 and 56-69 were elected and are currently pending. Claims 17, 31,32, 68 and 69 are canceled herein by amendment and without prejudice to Applicants' rights to pursue these claims in other patent applications.

## Amendments to the Specification

Examiner objected to and requested correction of the abstract of the disclosure because it is not a single paragraph pursuant to 35 U.S.C. §112, MPEP §608.01(b)(C). The abstract of the disclosure has been rewritten as a single paragraph as per Examiner's request to comply with 35 U.S.C. §112, MPEP §608.01(b)(C).

Applicant has also corrected a typographical error in the Roth et al. reference in the paragraph beginning on line 19 of page 2 and extending to line 3 of page 3.

### Amendments to the Claims

Applicant has currently amended Claims 1, 3, 16, 18,19, 20, 56 and 57. As noted above, Claims 17, 31,32, 68 and 69 are canceled herein by amendment and without prejudice to Applicants' rights to pursue these claims in other patent applications.

### Claim Rejections under 35 U.S.C. §112, first paragraph

Examiner rejected Claims 1-32 and 56-69 under 35 U.S.C. §112, first paragraph, alleging that the specification, while being enabling for extending the lifespan of mice which comprises the administration of C(sub)3 tris malonic acid C(sub)60, does not reasonably provide enablement for extending the lifespan of metazoans or metazoan cells in general which comprises the administration of all of the claimed C(sub)60 compounds, (e.g., claim 1), "a superoxide dismutase-mimetic" (Claim 16) or "an antioxidant" (Claims 31 and 68) generally.

Examiner further doubts the objective truth of the statement that the lifespan of a metazoan or a metazoan cell in general may be extended through the administration of a C(sub)60 compound (e.g., claim 1), "a superoxide dismutase-mimetic" (Claim 16) or "an antioxidant" (Claims 31 and 68) because "the art establishes that lifespan extension may be accomplished in only two specific types of metazoa by only two specific means." Examiner particularly points to teachings by Roth et al. (in *European Journal of Clinical Nutrition*, 2000; and *Annals New York Academy of Science*, 2001) for the proposition that dietary energy restriction is "the only proven method" for extending lifespan and slowing aging in mammals. Examiner also cites teachings by Kitani et al (*Life Sciences*, 1992) that with respect to studies of pharmacological intervention in the lifespan of animals (e.g., rats) "no single pharmaceutical or chemical agent has been shown to be reproducibly effective in this regard." In summary, the Examiner has concluded that lifespan extension may be accomplished in only two specific types of metazoa by only two specific means and has alleged lack of enablement for metazoan organisms besides mice, lack of enablement for compounds other than C(sub)3 tris malonic acid C60, and lack of enablement for superoxide dismutase-mimetics or anti-oxidants.

### Enablement of increased longevity in organisms besides mice

In responding to the Examiner's conclusion that the art recognizes only two means of increasing lifespan based on the quotations of Roth et al (2000) and Kitani et al (1992), Applicant first notes that both references significantly pre-date this Application and that both written statements were made in ignorance of the data disclosed in this Application filed in 2002 that clearly demonstrates lifespan increases in mice with a non-metallic SOD (super oxide dismutase) mimetic (Example 2). Furthermore, additional means of increasing lifespan such as use of 2-deoxyglucose (Roth et al. 2001), increasing both superoxide dismutase and catalase

levels (Sohal and Weindruch, 1996; IDS submitted with this filing), and increasing superoxide dismutase activity alone (Melov et al, 2000; IDS submitted with this filing) are recognized in the art. Finally, the art has also recognized that the lifespans of a variety of organisms such as mice, rats, roundworms, fruit flies, *Daphnia* (water fleas), fish, and spiders can be increased by various means (Sohal and Weindruch, 1996).

With respect to enablement of the instant invention, the mouse system used in demonstrating the instant invention is recognized in the art as a well documented system for identifying treatments that result in a longevity increases in a variety of organisms. Mice are one of the four standard species used for lifespan studies, with the roundworm *C.elegans*, the fruit fly *Drosophila* and rats being the other three. The National Institute of Aging, a division of the National Institutes of Health, has funded an "Interventions Testing Program" to test anti-aging drugs or treatments, and specifically chose mice as the species most likely to provide information that could be translated to humans (see <a href="http://www.nia.nih.gov/ResearchInformation/ScientificResources/InterventionsTestingProgram.htm">http://www.nia.nih.gov/ResearchInformation/ScientificResources/InterventionsTestingProgram.httm</a>; IDS submitted with this filing). This trial uses lifespan extension in mice as the principal outcome measure to determine efficacy of anti-aging treatments or interventions. Mice have also been used to identify biomarkers of aging for use in mammals such as humans (see Turturro et al, 1999; IDS submitted with this filing). Thus, it is clear that mice are regarded as a valid mammalian model system for demonstrating longevity effects that are expected to carry over to other organisms.

Having established that a valid experimental system was used to demonstrate longevity effects in the instant application and in response to the Examiner's comments regarding reasoned

scientific statements that support of enablement (page 6 of January 18<sup>th</sup> Office Action), Applicants also note that there is scientific evidence that the particular treatment disclosed by the applicant will result in lifespan increases in multiple organisms. The examiner has acknowledged that anti-aging treatments based on caloric restriction work in mice and a variety of other organisms. (see Sohal and Weindruch, 1996; Lee et al., 1999; Wang et al., 2004; IDS submitted with this filing). Deprenyl is another longevity enhancing treatment that is effective in mice and other organisms (e.g., Knoll, 1988; Kitani et al., 1992; Carillo et al., 2000; Jordens et al., 1999; previously submitted IDS). A common feature of both caloric restriction and deprenyl treatments shown to increase longevity in a variety of organisms is that both treatments may involve reductions in oxidative stress (Sohal and Weindruch, 1996; Jordens et al., 1999; Carrillo et al., 2000). This is especially significant with respect to this Application, since the disclosed use of a non-metallic SOD mimetic is expected to exert its lifespan increasing effects by reducing oxidative stress. The exemplary non-metallic SOD mimetic compound of this invention, C(sub)3 tris malonic acid C(sub)60, clearly functions in vivo as a superoxide dismutase mimetic as it has been demonstrated to rescue mice with mutations in their endogenous Sod2 (mitochondrial superoxide dismutase) gene (Ali et al., 2004; IDS submitted with this filing). The application demonstrates both in vitro SOD activity as well as at least some catalase activity of C(sub)3 tris malonic acid C(sub)60 (Example 4, pages 22-26). As acknowledged by the examiner, the Applicants do disclose increased longevity of mice treated with the non-metallic SOD mimetic C(sub)3 tris malonic acid C(sub)60 (Figure 4). Reducing oxidative stress by increasing both SOD and catalase activity has also been shown to increase longevity in transgenic fruit flies (Sohal and Weindruch, 1996). Treatment of the round worm C. elegans with two metallic superoxide dismutase mimetics increased longevity in one study (Melov et al, 2000; IDS submitted with this filing) but did not increase longevity in another study (Keaney et al, 2004;

IDS submitted with this filing). However, other studies of *C.elegans* with mutations in genes that cause increases in the levels of endogenous superoxide dismutase and/or catalase also note a correlation of resistance to oxidative stress with increased life span in *C.elegans* (Larsen, 1993; Honda and Honda, 2002; both in IDS submitted with this filing). In summary, increasing superoxide dismutase activity, as taught in the Application, has been demonstrated by the Applicants to increase longevity in widely accepted model mammalian organism and appears to involve a common mechanism (i.e. reduction of oxidative stress) associated with other treatments shown to increase longevity in multiple metazoan organisms (i.e. caloric restriction and deprenyl treatment). Applicants therefore submit that they have met the enablement requirement with respect to claims directed to increasing the lifespan of metazoan organisms.

Finally, in considering enablement of the invention in organisms besides mice,

Applicants note that to meet the enablement requirement, it is only necessary that "the specification teaches those in the art enough that they can make and use the invention without "undue experimentation." Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1334

(Fed. Cir. 2003), citing Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365

(Fed.Cir.1997); In re Vaeck, 947 F.2d 488, 495, (Fed.Cir.1991). Applicants submit that the instant application provides clear guidance on how to make and administer the compounds of the invention to metazoans (including humans) and additionally provide evidence of how to administer the compounds of the invention to a standard model metazoan (i.e. mice). Guidance on making the compounds of the instant invention is clearly found in the description for synthesis of carboxyfullerene compounds in Example 1. Guidance for using the compounds of the instant invention are additionally found for mammals such as humans in the descriptions of administration methods, formulations and dosages on Page 13, line 20 through Page 16, line 9 of

the specification. The Applicants provide further enabling disclosure on use of the compounds of the invention in mammals and other metazoans by demonstrating the absence of toxicity of a 10mg/kg dose of a C<sub>3</sub> tris malonic acid C60 in two species of rats as shown in Example 3. Finally, provision of an enabling disclosure is further evidenced by reduction to practice of the invention in mice, a model mammalian organism, as shown in Example 2. Given this information, an individual skilled in the art need only apply routine experimentation to make and use the invention in a variety of metazoan organisms.

### Enablement of C(sub)60 derivitives other than C(sub)3 tris malonic acid C(sub)60

In rebutting the Examiner's rejection of the pending claims directed to C(sub)60 derivatives other than C(sub)3 tris malonic acid C(sub)60 for lack of enablement, Applicants have provided objective evidence in the form of an Affidavit under 37 CFR§1.132 that the Application was in fact enabling for derivatives other than the exemplary C(sub)3 tris malonic acid C(sub)60 compound at the time of filing. First, the Application incorporates by reference the work of Choi et al showing that C(sub)60 derivatives with either 1, 2, or 3 malonic acid groups (i.e., X=1, 2, or 3 in the nomenclature of the currently pending Claim 1 directed to the enabled genus of C(sub)60 derivatives) are effective free radical scavengers and that the C(sub)60 derivatives with 3 malonic acid groups reduce neuronal cell death under conditions known to stimulate oxidative stress (i.e. AMPA or NMDA treatment). Second, the Applicant has also declared in the accompanying Affidavit under 37CFR§1.132 that prior to the filing of the application, they had demonstrated that the C(sub)60 derivatives referred to as "C(sub)3", "Penta", "Tetra's" and "C(sub)3-lite" exhibited superoxide dismutase activity. This statement is supported in part by the notebook page shown in exhibit A2 of the Affidavit describing superoxide dismutase activity assays that is dated 11/23/99 and initialed by the Affiant. Also

note that the "C(sub)3", "Penta", "Tetra's" and "C(sub)3-lite" compounds represent compounds where R is either a carboxylic acid group ("C(sub)3"), a carboxylic acid or a hydrogen ("Penta", "Tetra's") or a hydrogen ("C(sub)3-lite") in the nomenclature of currently pending Claim 1 directed to the enabled genus of C(sub)60 derivatives. Furthermore, the Applicant has also declared that the "C(sub)3", "Penta", and "C(sub)3-lite" derivatives of carboxyfullerene were also shown to reduce NMDA receptor toxicity, a form of neuronal cell death mediated by mitochondrial superoxide production. These statements are supported in part by the initialed and dated notebook pages shown in exhibits A4 through A7 as well as in the computer output file shown in Exhibit A10 listing the times that raw data files corresponding to these experiments were entered as 11/14/99. Also note that the "C(sub)3", "Penta", and "C(sub)3-lite" compounds shown to reduce neuronal cell death represent compounds where R is either a carboxylic acid group ("C(sub)3"), a carboxylic acid or a hydrogen ("Penta", "Tetra's") or a hydrogen ("C(sub)3-lite") in the nomenclature of currently pending Claim 1 directed to the enabled genus of C(sub)60 derivatives.

Several lines of evidence support the conclusion that the instant application enables one skilled in the art at the time of filing to practice the invention with C(sub)60 derivatives other than C(sub)3 tris malonic acid C(sub)60, and more specifically for C(sub)60 derivatives where R is independently selected from the group consisting of –COOH and -H, and wherein X is at least 1 in the nomenclature of currently pending Claim 1. First, that reductions in oxidative stress are correlated with increases in lifespan were clearly appreciated by the Applicants at the time of filing as evidenced by the discussion on page 6, lines 7-14 of the specification. Second, the Applicant had demonstrated at the time of filing that a variety of chemically related C(sub)60 derivatives possessed a chemical activity (i.e. a non-metallic superoxide dismutase activity)

known to reduce oxidative stress. Third, the Applicants have demonstrated at the time of filing that a variety of chemically related C(sub)60 derivatives could inhibit an *in vivo* oxidative stress mediated process (i.e. NMDA receptor-mediated neuronal cell toxicity) in cultured cells. Finally, the Applicants demonstrated that an exemplary C(sub)60 compound (C(sub)3 tris malonic acid C(sub)60) that has the same superoxide dismutase and *in vivo* oxidative stress inhibiting capabilities as the other C(sub)60 derivatives was also capable of increasing lifespan in mice. Consequently, the conclusion that C(sub)60 derivatives other than C(sub)3 tris malonic acid C(sub)60 were enabled at the time of filing is supported by evidence that C(sub)3 tris malonic acid C(sub)60 and the other C(sub)60 derivatives share the same key properties (i.e. non-metallic superoxide dismutase activity and inhibition of oxidative stress *in vivo*) that appear to be responsible for the observed increases in lifespan caused by C(sub)3 tris malonic acid C(sub)60.

## Enablement of non-metallic superoxide dismutase mimetics

With respect to the Examiners rejection of Claim 16 and its' dependent claims over the lack of enablement of "superoxide dismutase-mimetics", the currently amended Claim 16 and its dependent claims now recite a <u>non-metallic</u> superoxide dismutase-mimetic. Support for this claim amendment is found at least in the originally presented Claim 17 which claimed "The process of Claim 16 wherein said superoxide dismutase-mimetic comprises a non-metallic compound." Further support for this amendment is found on page 6, lines 22 and 23 which states: "Still, a further embodiment of the instant invention comprises a non-metal containing composition which can catalytically eliminate two biologically reactive species." The specification also describes novel properties and advantages of the non-metal containing super oxide dismutase-mimetics relative to metallic superoxide dismutases, such as the ability to

catalytically eliminate two biologically reactive and physiologically relevant species, superoxide and hydrogen peroxide (page 12, lines 9-15; page 17, lines 5-9 and 10-14). As noted above, enablement of the exemplary non-metallic super oxide dismutase-mimetics "C(sub)3", "Penta", "Tetra's" and "C(sub)3-lite" was variously demonstrated with respect to chemical activity (super oxide dismutase activity), inhibition of oxidative stress *in vivo* (inhibition of neuronal cell death), and lifespan increases. Applicant therefore submits that the claims to <u>non-metallic</u> superoxide dismutase mimetics are fully enabled by the specification.

# Claim Rejection 35 U.S.C. §112, Second Paragraph

- 1. Examiner rejected Claims 1-4, 6-15, 19-21, 32, 56-59, 61-67, and 69 as being indefinite because the language employed in Claims 1, 19, 32, 56, and 69, does not accurately describe the carboxyfullerene compounds intended for use in the presently claimed invention. To address this rejection, the Applicants have amended the claims to include a structural drawing of the compounds of the invention and inserted the phrase "C is directly bonded to two adjacent carbons of C(sub)60 and". The Applicants believe that stating that C is directly bonded to two adjacent carbons of the C(sub)60 fullerene clearly indicates the type of bond found in the compounds of the invention and is consistent with the Examiner's suggestions (page 10 of the January 18, 2005 Office Action). Further support for the amendments to Claims 1, 19 and 56 as presented herein can be found in the structural depictions of the compounds shown in the original Figure 2 of the specification.
- II. Examiner rejected Claims 8, 10, 20, 25, 27, 57, 63, and 65 under 35 U.S.C. §112, second paragraph as indefinite because the term "about" in the expressions "about 3 mg/kg", "about 15 mg/kg" and "about 4" in these claims is a relative term which renders the claim indefinite.

17

According to the Federal Circuit,

"broadening usages as 'about' must be given reasonable scope; they must be viewed by the decision maker as they would be understood by persons experienced in the field of the invention... Although it is rarely feasible to attach a precise limit to 'about,' the usage can usually be understood in light of the technology embodied in the invention. When the claims are applied to an accused device, it is a question of technologic fact whether the accused device meets a reasonable meaning of 'about' in the particular circumstances." *Modine Mfg. Co. v. United States Int'l Trade Comm'n*, 75 F.3d 1545, 1554 (Fed. Cir. 1996); see also, Merck & Co. v. Teva Pharmaceuticals USA Inc., 395 F.3d 1364, 1372 (Fed. Cir. 2005) (holding "the term 'about' should be given its ordinary and accepted meaning of 'approximately' unless patentee clearly redefines 'about' in the specification.").

Applicants respectfully submit that the application expressions "about 3 mg/kg" and "about 15 mg/kg" to Claims 8, 10, 25, 27, 63, and 65 are not indefinite under 35 U.S.C. §112, second paragraph because a skilled practitioner in the pharmaceutical arts to which this Application is directed would understand the meaning of the term "about" with regard these particular claims directed to the dosing of patients or animals. Optimization of dosages of pharmaceuticals is in fact routine experimentation for a skilled practitioner of the pharmaceutical arts. The term "about" in reference to dosing is also consistent with the specifications statement that "The oral dosages contemplated in accordance with the present invention will vary in accordance with the needs of the individual patient as determined by the prescribing physician" (page 15, lines 3-5). Applicants therefore request that the Examiner withdraw the rejections to Claims 8, 10, 25, 27, 63, and 65 under 35 U.S.C. §112, second paragraph. Finally, the rejection of Claims 20 and 57 for the expression "about 4" is rendered moot by the current amendments of those claims that remove the word "about".

### Claim Rejections under 35 U.S.C. §103

# I. Joint Inventors

Applicant acknowledges their obligation under 37 CFR§1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §102(e), (f), or (g) prior art under 35 U.S.C. §103(a). To Applicants' best knowledge, all subject matter of the claims of the instant invention was commonly owned at the time of invention of each of the claims.

II. Unpatentable over Lei et al. and Stedman's Medical Dictionary in view of Chiang, Choi et al. and WO 97/46227.

Examiner rejected Claims 1-32 and 56-69 under 35 U.S.C. §103(a) as being unpatentable over Lei et al. (U.S. Patent No. 6,777,445, cited by Examiner) and Stedman's Medical Dictionary (cited by Examiner) in view of Chiang (U.S. Patent No. 5,648,523, cited by Examiner), Choi et al. ((U.S. Patent No. 6,265,443, cited by Applicants) and WO 97/46227 ("WO '227", PCT counterpart of Choi et al. '443, cited by Applicants).

To establish obviousness, the Examiner must first establish one skilled in the art would have had a suggestion or motivation to combine the cited references. In addition, should the Examiner establish sufficient suggestion or motivation to combine the references, the Examiner must also show a reasonable expectation that the combination would be successful. Finally, the prior art references must teach or suggest all of the claim limitations. Here, there is no motivation or suggestion to combine the cited references to extend lifespan, the references themselves provide no reasonable expectation that the compounds would have extended lifespan, and the references do not teach or suggest the key claim limitation of extending the lifespan of a metazoan or metazoan cells.

First, there is no suggestion or motivation to combine the references cited by the Examiner. One of ordinary skill in the art would not be motivated look to references such as Lei et al. pertaining to the subject matter of the treatment of viral and/or bacterial infections when developing methods for prolonging the lifespan or duration of metazoans or metazoan cells. Specifically, Lei et al. demonstrates only the use of C(sub)3 as a treatment for viral and/or bacterial infection of mice, not to increase the lifespan of normal, uninfected mice. The treatments of Lei et al. resulted in increased survival, not lifespan. The term "lifespan" is erroneously used in Lei et al. to indicate survival following infection and does not have the same meaning of the term "lifespan" as used in Applicants' invention or by active practitioners in the field of aging (see for example Wang et al., 2004; cited in the currently submitted IDS). The terms "lifespan" and "survival" have specific and distinct meanings to practitioners in the field of aging. In the Application itself, "lifespan" is defined as "the average expected length of life of a kind of organism or cell in a particular environment" (page 16 lines 10-14). In contrast, "survival" is the period of time or the number of animals that live after an insult (injury, infection, etc.). Thus Lei et al. demonstrate that treatment of a viral and/or bacterial infection with C(sub)3 increases survival from the disease, but do not demonstrate or suggest that C(sub)3 can increase the *lifespan* of a normal animal. In fact, Lei et al. does not appear to contain any experiments that were designed or could be interpreted to reveal lifespan increasing effects (i.e. a comparison of the lifespan of treated and untreated uninfected mice). In contrast, Applicants demonstrate that treatment with non-metallic superoxide dismutase inhibitors increase the lifespan of normal, healthy animals and additionally provides evidence that an exemplary compound produces such results. Like Lei et al., the Choi et al. reference uses fullerene derivatives, including buckminsterfullerene, in the treatment of disease, not for

prolonging the lifespan of healthy, normal organisms. Specifically, Choi et al. teaches a method of treating *neurotoxic injury*. Choi et al. also does not appear to contain any experiments that were designed or could be interpreted to reveal lifespan increasing effects (i.e. a comparison of the lifespan of treated and untreated uninfected mice). It is not at all clear that one skilled in the art would have had any suggestion or motivation to combine references such as Lei et al and Choi et al that disclose completely distinct and unrelated uses (i.e. treatment of infections and treatment of neurotoxicity). Therefore, Applicants respectfully submit that their process for prolonging the length or duration of the expected lifespan of metazoans or metazoan cells is not obvious as one skilled in the art would have had no motivation or suggestion to combine disclosed methods of increasing the survival of animals suffering from viral and/or bacterial infections (Lei et al.) or of treating neurotoxic injury (Choi et al) to arrive at a method of increasing the lifespan of healthy, normal organisms.

The references cited by the Examiner also do not provide a reasonable expectation that the combination would be successful in increasing the life span of an animal. As noted in the above discussion, the Lei and Choi et al references were respectively directed to treatments of viral and/or bacterial infections and neurotoxic injury and did not include experiments that were designed or could be interpreted to reveal lifespan increasing effects (i.e. a comparison of the lifespan of treated and untreated uninfected mice). Absent the Applicants' demonstration through the suitably designed experiments in Example 2 of the specification that an exemplary non-metallic superoxide dismutase inhibitor treatment increased lifespan, one skilled in the art would have had no reasonable expectation that the C(sub)3 treatments shown by Lei et al and Choi et al to be effective in treating viral and/or bacterial infections and neurotoxic injury would yield lifespan increases.

Finally, the combination of cited references fail to disclose or suggest the key claim limitation of extending the lifespan of a metazoan or metazoan cells. As discussed above, the Lei et al. and Choi et al. references were respectively directed to treatments of viral and/or bacterial infections and neurotoxic injury and neither explicitly disclose or suggest use of C(sub)3 to increase lifespan. Lei et al. in fact disclose a wide variety of biological activities of fullerene derivatives such as use in photodynamic therapy; as inhibitors of HIV-1 protease; as neuroprotective agents; as antiapoptotic agents; as protective agents against iron-induced oxidative stress; or as an in vitro antibacterial agent ('445 Patent, col. 1 line 59 to col. 2 line 6) but conspicuously omit mention of use as a lifespan increasing agent. Similarly, Chiang et al. recite a long list of prophesized clinical uses of fullerenes including cancer treatment, diabetes, neurodegenerative diseases, and inhibition of restenosis (Column 6, lines 15-23) yet fail to mention use as a lifespan increasing agent. Applicant therefore submits that the references do not teach or suggest the key claim limitation of increasing lifespan. For these reasons and those cited above, the Applicant submits that the rejection of the currently pending claims under 35U.S.C.\(\frac{8}{103}\) is improper and request that it be withdrawn.

### Non-Statutory Provisional Double Patenting Rejection

Previously presented and currently pending Claims 1, 4-32 and 56-69 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 22-33 of copending U.S. Patent Application No. 10/373,425.

Applicant respectfully requests that this provisional rejection be held in abeyance until such time as claims in the instant application are found to be allowable.

### **CONCLUSION**

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant respectfully requests that the Examiner reconsider and withdraw each rejection. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that a personal communication will expedite prosecution of this application, he is invited to telephone the undersigned agent at the number provided.

Prompt and favorable consideration of this Response is respectfully requested.

Respectfully submitted,

Charles P. Romano, Reg. No. 56,991

Thompson Coburn LLP One US Bank Plaza St. Louis, MO 63101 314-552-6255

314-552-7255 (Fax)